

11.2  
604. optical element 22 disposed substantially in a plane 24 conjugate to a planar back aperture 28 of the focusing lens 12 into the subject cell.

For this implementation to be generally useful, it would be necessary to alternate turning on the beam altering optical element 22 and laser 102 to create traps and then turning off the laser and beam altering optical element 22 to create images.

**Page 9, please replace the fourth full paragraph, continuing to page 10, with the following new paragraph:**

11.3  
When the laser beam 100 is directed through the beam altering optical element 22, the beam altering optical element produces a plurality of beamlets having an altered phase profile. Depending on the number and type of optical traps desired, the alteration may include refraction, diffraction, wavefront shaping, phase shifting, steering, diverging and converging,. Thus, the laser beam 100 proceeds from area A' on the beam splitter 30 to area A on the beam altering optical element 22 and through area B at the back aperture 28 of the focusing lens 12 thereby effectively overlapping all the *beamlets* at the back aperture of the focusing lens. The *beamlets* are then converged as the pass through the focusing lens 12 thereby producing the optical gradient conditions necessary to form the optical traps.

**Page 10, please replace the third full paragraph with the following new paragraph:**

11.4  
Examples of suitable dynamic beam altering optical elements having a time dependent aspect to their function include computer generated diffractive patterns, phase shifting materials, liquid crystal phase shifting arrays, micro-mirror arrays, piston mode micro-mirror arrays, spatial light modulators, electro-optic deflectors, acousto-optic modulators, deformable mirrors, reflective MEMS arrays and the like. With a dynamic beam altering optical element, the media which comprises the beam altering optical

A4  
cont. element can be altered, to change the phase pattern imparted to the focused beam of light which results in a corresponding change in the phase profile of the focused beam of light, such refraction, diffraction, or convergence.

**Page 11, please replace the first paragraph with the following new paragraph:**

125 The beam altering optical element is also useful to impart a particular topological mode to the laser light. Accordingly, one *beamlet* may be formed in a helical mode while another *beamlet* is formed in a Gaussian mode.

**Page 11, please replace the fourth and fifth paragraphs, continuing to page 12, with the following new paragraphs:**

176 One example of an application of the system illustrated in FIG. 3A is to troll the probes through the media 3000 (FIG. 1) containing the targets T1-T5. (FIG. 1) By containing the probes optically, as opposed to physically, and moving the probes within the subject cell 10 the opportunity for interaction of a probe with each target is increased, thus improving the speed and efficiency of the assay.

Another example of an application of the system illustrated in FIG. 3A is that upon completion of the assay, selection can be made, via computer 38 and/or operator 36, of which probes to discard and which to collect. The re-configurable nature of the array allows for selective movement of a given optical trap and contained probe. In some cases the media 3000 and unbound targets will be removed or flushed from the subject cell 10 through an outlet port 18 and the assay will be completed. In other cases at least some of the probes still contained by optical traps, are reused with additional targets to perform further assays. This technique can be useful in the case of probes that tested positive or negative, depending on the parameters of the assay. In yet other cases, because the array of probes is re-configurable as to the

quantity and quality of probes forming the array, the optical traps can be used to discard unbound probes and acquire additional probes for further experimentation.

**Page 12, please replace the first full paragraph with the following new paragraph:**

Another example of an application of the system illustrated in FIG. 3A is to interrogate cells by spectrum and create an array of probes from selected interrogated cells. Spectroscopy of a sample of biological material can be accomplished with an imaging illumination 39 suitable for either inelastic spectroscopy or polarized light back scattering, the former being useful for assessing chemical structure, and the latter being suited for measuring nucleus size. For instance, a computer 38 can be used to analyze the spectral data and to identify suspected cancerous, pre-cancerous and/or non-cancerous cells and direct optical traps to contain selected cell types. The contained cells may then be used as the probes in further assays such as the interaction of other biological material, cells, antibodies, antigens, drugs or chemicals on the probes. Those skilled in the art will recognize that the methodology used to interrogate and concentrate cells based on parameters specific to cancerous cells, may be altered, without departing from the scope of the invention, for use with interrogating and or separating blastomeres, cells, or other material as called out for in the protocol of an assay.

**Page 12, please replace the second full paragraph with the following new paragraph:**

Another example of an application of the system illustrated in FIG. 3A is for investigating targets by spectrum. The spectrum of those probes which had positive results (have bound targets) can be obtained by using imaging illumination 39 such as that suitable for either inelastic spectroscopy or polarized light back scattering. The computer 38 can analyze the spectral data to identify the desired targets and direct the optical array to segregate those desired targets. Those skilled in the art will

1.8  
cont. recognize that the methodology use to segregate targets based on spectral data may be altered, without departing from the scope of the invention, to identify and or segregate targets based on other information obtainable from the targets and or the optical data stream. The wavelengths of the laser beam 100 used to form arrays for investigating biological material include the infrared, near infrared, visible green, visible red, and visible blue from about 400 nm to about 1.06 mm.

**Page 12, please replace the third full paragraph, continuing to page 13, with the following new paragraph:**

119 An additional example of an application of the array is the use of a static, transmissive beam altering optical element to direct the array. The static beam altering optical element 40, such as a hologram or grating, as illustrated in FIG. 4 can be used to form a pre-determined range of optical traps. Using the static beam altering element 40 in situations where limited movement and/or reconfiguration of the array is adequate has the advantage of not requiring the computer processing power necessary to calculate the varying phase pattern available with a dynamic beam altering optical element. Although the static transmissive beam altering optical element illustrated in FIG. 4 is shown with a fixed surface 41 and discrete regions 42-26, a static beam altering optical element, either transmissive or reflective, may also have a substantially continuously varying non-homogenous surface, or a combination of discrete regions, and substantially continuously varying regions.

**Page 13, please replace the second full paragraph with the following new paragraph:**

File To move the probes 500-502 from position one P1 to position two P2, the static beam altering optical element 40 is rotated around a spindle 47 (which may be attached to a controlled motor (not shown)) to align the laser beam with region two 43 which will generate the second set of optical traps at

P10  
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position two P2. By constructing the second set of optical traps in the appropriate proximity to the former location of the first set of optical traps the probes can be passed from set of optical traps to set of optical traps. The sequence may continue passing the probes from position two P2 to position three P3, from position three P3 to position four P4, and from position four to position five P5 by the rotation of the beam altering optical element to align the appropriate region 42-46 corresponding to the desired position P1-P5. The time interval between the termination of one set of optical traps and generation of the next should be adequate to allow passage of the probes before they drift. One use of this system, as described within, is to troll the probes through the media thereby providing opportunity to have targets within the media interact with the probes. This type of simple movement may also be useful in moving the probes from a sub-cell 16 (FIG. 1) to another area of the subject cell 10, or segregating probes into a sub-cell 16.

**Page 15, please replace the first full paragraph with the following new paragraph:**

P11

To generate the optical traps, a laser beam is directed through a fiber optic cable 150 out a collimator end 151 and reflected off the dynamic surface 59 of the optical element 51. The beam of light (not shown) exiting the collimator end 151 of the fiber optic 150 is diffracted by the active surface 59 of the optical element 51 into a plurality of beamlets (not shown). The beamlets then reflect off the first mirror M1 through the first set of transfer optics TO1 down the first light channel 53a through the second set of transfer optics TO2 to the second mirror M2; and are directed at the dichroic mirror 58 up to the back aperture 57 of the objective lens 56, are converged through the objective lens 56, thereby producing the optical gradient conditions necessary to form the optical traps.

**Page 15, after the fourth full paragraph, insert the following new paragraph:**

P12

FIG. 3B shows a variation on FIG. 3A. FIG. 3B shows a holographic optical tweezer